REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
22/02/2018	poster	02/22/2018-02/23/2018

4. TITLE AND SUBTITLE
An Elusive Diagnosis Following Cardiac Arrest

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Fullam, Capt Timothy R.

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
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210-292-7141

8. PERFORMING ORGANIZATION REPORT NUMBER
17573

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
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210-292-7141

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release. Distribution is unlimited.

13. SUPPLEMENTARY NOTES
40th Annual Carrell-Krusen Neuromuscular Symposium, Dallas TX, 22-23 February 2018

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Clarice Longoria
					19b. TELEPHONE NUMBER *(Include area code)* 210-292-7141

An Elusive Diagnosis Following Cardiac Arrest

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**The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components*

Case Presentation

49-year-old female was admitted after found unresponsive in bed. Cardiopulmonary resuscitation (CPR) was initiated by the husband followed by emergency medical services (EMS) who diagnosed ventricular fibrillation. She was intubated and advanced cardiac life support administered with return of spontaneous circulation (ROSC) in the emergency department. Amiodarone was loaded and maintenance initiated. Workup for etiology of her ventricular fibrillation, including computed tomography (CT) of the head and CT angiogram of the pulmonary arteries, was negative. Left heart catheterization and ventriculography demonstrated no evidence for coronary artery disease, a reduced ejection fraction (EF) with global hypokinesis and dilated left ventricle. Episodes of ventricular tachycardia continued causing recurrent arrests with concomitant worsening metabolic acidosis and cardiac function. She was transitioned to venous-arterial extracorporeal membrane oxygenation (VA ECMO) with improved arrhythmias and metabolic acidosis but continued cardiogenic shock and increasing vasopressor requirements. Given concern for potential myocarditis and need for a left ventricular assist device (LVAD) or cardiac transplant, she was transferred to an outside hospital for further care.

Myocardial biopsy was negative for inflammatory changes consistent with myocarditis. Her hemodynamic stability and cardiac function improved from a nadir EF of 10-15% to 40-50% after 8 days of ECMO. While at the facility, she was treated with intermittent cisatracurium (Nimbex®), dexmedetomidine (Precedex®), and fentanyl. ECMO was discontinued and she was transferred back to our hospital given no further need for LVAD or transplant. Cisatracurium was discontinued prior to transfer and dexmedetomidine and fentanyl were discontinued on arrival. Due to persistent flaccid paralysis and inability to follow commands, Neurology was consulted

Neurology Consultation/Exam

Additional History Obtained: Bilateral cataract removal over the past year reported by husband, mother of 3 healthy adolescent children with no history of miscarriage

MS: Would attend to examiners when her name was spoken. Would not follow any simple commands to stick out tongue or close eyes and inconsistently appears to track to command

CN: Bilateral ptosis of eyelids with inability to fully close eyes; bilateral temporal wasting noted. Otherwise grossly intact.

Motor/Sensation: Flaccid bilateral upper and lower extremities. 0/5 strength with volitional movement but with deep nailbed pressure patient able to withdraw both lower extremities against gravity

Reflexes:	bi	tri	BR	pat	Achilles	plantar
R	2-	2-	2-	0	0	equivocal
L	2-	2-	2-	0	0	down

- Trace/Possible Percussion myotonia of L thenar eminence

Gait: Unable to obtain.

Inpatient Evaluations/Studies

Serum Studies: Na 150 (down-trending from high of 158), NH3, TSH, CK, Lactate, VBG WNL
CSF Studies: Unremarkable
EEG: Abnormal EEG (Awake, Drowsy, ATE): Slowing, continuous, generalized, theta-delta
MRI Brain w/wo contrast: No acute intracranial abnormality
Train of Four: No evidence for persistent neuromuscular blockade
NCS/EMG:
NCS, including repetitive stimulation, unremarkable

Muscle	Ins	Spontaneous Activity			Voluntary Act				Comments
	Activity	Fibs	Fasc	Other	Recruitment	Dur	Amp	Poly	
Tibialis anterior.L	Incr	-	-		-	Short ++	Low ++	25%	
Vastus lateralis.L	NML	-	-						No activation
Abductor pollicis brevis.L	Incr	2+	-						No activation
1st dorsal interosseous.L	Incr	-	2+						No activation
Biceps brachii.L	NML	-	-						No activation

DMPK Gene Analysis: 12 CTG Repeats on both alleles (No evidence of a repeat expansion identified)
CNBP Gene Analysis: No evidence of repeat expansion in the CNBP gene detected

4 Month Follow-Up

Repeat examination (notable findings):
- Bilateral ptosis with no fatigability, bilateral weakness of orbicularis oculi as well as cheek puff/lip pursing, Neck Flexion/Extension 4/5.
- Significant atrophy of bilateral temporalis muscles
- diffusely decreased bulk with strength as follows:

Upper:	Del	Tri	Bi	WE	WF	FE	FF	HI
Right	5/5	5-/5	5-/5	5/5	5/5	5-/5	5/5	4/5
Left	5/5	5-/5	5-/5	5/5	5/5	5-/5	5/5	4/5

Lower:	HF	KE	KF	ADF	APF	EHL
Right	4+/5	5/5	5/5	4+/5	4+/5	4+/5
Left	4+/5	5/5	5/5	4+/5	4+/5	4+/5

-Reflexes 1/4 in bilateral upper extremities, absent at the patella and Achilles' bilaterally, trace percussion myotonia of thenar eminence on left but absent at extensor compartment of forearm and tongue
-Gait with exaggerated lordosis and 'waddling' type pattern

Final Workup/Diagnosis

Repeat EMG:

Muscle	Ins Act	Spontaneous Activity			Voluntary Motor Unit Potentials			
		Fibs	Fasc	Other	Recruitment	Dur	Amp	Poly
Deltoid.R	NML	-	-		NML	NML	NML	None
Triceps brachii (Lateral head).R	Inc	1+	-	Myot	NML	Long +	High +	25%
Flexor digitorum profundus, dig 4 & 5.R	Inc	1+	-	Myot	Rapid +	Short +	Low +	75%
Sternocleidomastoid.R	Inc	-	-	Myot	NML	Short +	Low +	25%
Tibialis anterior.R	Inc	-	-		NML	Short +	Low +	15%
Gastrocnemius (Medial head).R	Inc	-	-	Myot	NML	Short +	Low +	None
Quadriceps.R	Inc	1+	-	Myot	NML	NML	NML	None
T7 paraspinal.R	NML	-	-		NML	NML	NML	None
T10 paraspinal R	NML	-	-		NML	NML	NML	None

DMPK Gene Analysis: 790 and 12 repeats (Pathogenic)
Amended Initial report: PCR Analysis with 12 CTG Repeats and Inconclusive allele 2
Southern blot (initial sample): 800-1300 CTG repeats on allele 2

Discussion

-Myotonic Dystrophy Type 1 is the most common muscular dystrophy of adulthood which affects between 1 per 8000-9000 individuals worldwide.
-Neuromuscular manifestations of myotonia and skeletal muscle disease may be subtle or overlooked by patients making exact onset of the disease difficult to ascertain and raises the possibility that a non-neurologist physician may be the first to evaluate these patients[1,2].
-EM is the result of decreased expression of muscle-specific chloride channel type 1 (CIC-1) due to abnormal RNA processing from toxic gain of function of the transcribed DMPK repeat protein [3,4].
-Membrane hyper-excitability can be curtailed by altering sodium channel opening frequency or duration which is the basis for mexilitine therapy for myotonia [5]. Our patient's lack of EM initially may be explained by the acute effects of amiodarone (shown to have Class IB antiarrhythmic properties acutely) versus her critical illness[6].
-Genetic testing has a low false negative rate, however, 3-5% of the DM1 population can have interrupting CCG, CTC, and CGG repeats within the CTG repeat which can cause false negative studies[7].
-A potential confounder is dilution of the sample sent for testing. Average ECMO patients require 2 to 3 packed red blood cells and up to 14 plasma units and cryoprecipitate daily which, in our patient, obscured her initial serum genetic testing [8].
-DM1 patients have a hypersensitivity to anesthetic agents with prolonged recovery from sedation and propensity for potential prolonged mechanical ventilation, which likely contributed to our patient's initial presentation and prolonged hospital course [9].
-This case re-affirms the importance of recognition of the stigmata of DM1, especially in care settings where the diagnosis may be missed. Typically, genetic testing and EMG/NCS can confirm the diagnosis; however, providers should be aware of potential false negatives to avoid abandoning the correct diagnosis in the face of initial negative results.

An Elusive Diagnosis Following Cardiac Arrest

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A 49-year-old female was admitted following ventricular fibrillation associated cardiac arrest with return of spontaneous circulation (ROSC) with advanced cardiac life support. Past medical and surgical history was notable for bilateral cataract removals over the preceding year. Family history was non-contributory. Workup for the arrest was unremarkable including computed tomography (CT) of the pulmonary arteries, left heart catheterization, and ventriculography. Her initial course was complicated by newly diagnosed dilated cardiomyopathy with reduced ejection fraction, ventricular tachycardia, and cardiogenic shock requiring venous-arterial extracorporeal membrane oxygenation (ECMO). Given concern for myocarditis, a myocardial biopsy was performed and negative for inflammatory changes. After discontinuation of ECMO, neurology was consulted due to failure to wean from the ventilator. Initial exam was significant for bilateral temporal wasting and ptosis with subtle percussion myotonia of the left thenar eminence. She had no volitional movement of her extremities and reflexes were hypoactive. Electroencephalogram and magnetic resonance imaging of the brain were unremarkable for seizure activity or evidence of anoxic injury, respectively. Given the findings of bilateral ptosis, possible percussion myotonia, temporal wasting, recent cardiac arrest, and early cataracts, a workup for myotonic dystrophy type I was pursued. Nerve conduction study and electromyography (NCS/EMG) did not demonstrate myotonic discharges and was only remarkable for reduced amplitudes of the left median and ulnar motor studies. DMPK gene analysis was negative, with only 12 CTG repeats. Follow up CNBP gene analysis for myotonic dystrophy type 2 (DM2) was also negative. The patient's mental status and clinical state improved and she was discharged to a rehabilitation facility after placement of an implantable cardioverter defibrillator 2 weeks after initial consultation. The patient returned for further evaluation after recovery from her acute illness and repeat clinical exam, EMG/NCS, and ultimately genetic testing confirmed the underlying diagnosis.